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In re Application of:

Confirmation No. 1639

Nelson

For:

Group: 1614

Serial No. 10/616,692

Examiner: Unassigned

Filed: July 9, 2003

Compositions and Methods for the

Treatment of Parkinson's Disease and

Tardive Dyskinesias

CERTIFICATE OF MAILING
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INFORMATION DISCLOSURE STATEMENT

Hon. Commissioner for Patents Alexandria, VA 22313-1450

Sir:

This application is a continuation-in-part of U.S. Application Serial No. 10/192,414 filed July 9, 2002, which is a continuation-in-part of U.S. Application Serial No. 09/615,639 filed July 13, 2002 (now U.S. patent 6,417,177). In compliance with the duty of disclosure set forth in 37 CFR 1.97, the Examiner is referred to the files of those applications for prior art of record. For the Examiner's convenience, copies of the 1449 forms in those cases are enclosed.

Additional references known to the applicants have been listed on additional PTO-1449 forms. This information is cited in a spirit of forthrightness and cooperation to enable the applicants to obtain that measure of protection for the invention to which there is entitlement. However, no representation is made that the listed art actually qualifies as prior art under the patent statute and the mere use of PTO-1449 is not an admission that all listed references are prior art. No representation is made that applicants know of the best art.

It is believed that this submission does not necessitate the payment of any fees; however, if this is incorrect, please charge any requisite fee to Deposit Account 07-1969.

Respectfully submitted,

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ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616/692	FILING DATE July 9, 2003	
APPLICANT J. Nelson		GROUP 1614	

U.S. PATENT DOCUMENTS

Exmr. Initial	Document Number	Date	Name	Class	Subclas s	Filing Date if Appropriate
	6,232,326	05/15/01	Nelson	514	336	
	5, 430,039	07/04/95	Roberts-Lewis et al.	514	297	

FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Subclas s	Translation Yes/No
				,		
						1

OTHER PRIOR ART (including Author, Title, Date, Pertinent Pages, etc.)

OTTENT RION ANT (including Author, Title, Date, Fertinent Fages, etc.)
Aisen, P.S., "Multicenter trial of hydroxychloroquine," CRISP (1998) abstract only
Allison, J. L., O'Brien, R. L. and Hahn, F. E., (1965), "Nature of thedeoxyribonucleic acid-chloroquine complex," <i>Antimicrob Agents Chemother</i> , 5:310-314
Amabeoku, G. J. and Chikuni, O. (1992), "Involvement of GABAnergic mechanisms in chloroquine-induced seizures in mice," <i>Gen Pharma</i> , 23(2):225-229
Amabeoku, G. J. (1994), "Some behavioral effects of chloroquine in rats suggesting dopaminergic activation," <i>Indian J Med Res</i> , 99: 87-94
Amabeoku, G. J. and Chikuni, O. (1992), "Chloroquine-induced seizures in mice: the role of dopaminergic system," <i>Br J Pharmacol</i> , 106: 54P, abstract only
Amabeoku, G. J. and Chikuni, O. (1992), "Chloroquine-induced seizures in mice: the role of monoaminergic mechanisms," <i>Eur J Neuropsychopharm</i> , 3 : 37-44
Augustijns, P. and Verbeke, N. (1992), "Stereoselectivity in the disposition of chloroquine and desethyl-chloroquine in rabbits," <i>Arzneimittelforschung</i> , 42(6):825-828
Augustijns, P., Geusens, P. and Verbeke, N. (1992), "Chloroquine levels in blood during chronic treatment of patients with rheumatoid arthritis," <i>Eur J Clin Pharmacol</i> , 42:429-433
Batchelor, P. E. et al. (1999), "Activated macrophages and microglia induced dopaminergic sprouting in the injured striatum and express brain derived neurotrophic factor and glial cell line derived neutrophic factor," <i>J Neurosci</i> , 19(5):1708-1716

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Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616/692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

	Batchelor, P. E. et al. (1999), "Activated macrophages and microglia induced dopaminergic sprouting in the injured striatum and express brain derived neurotrophic factor and glial cell line derived neutrophic factor," <i>J Neurosci</i> , 19(5):1708-1716
	Ben-Shachar, D. et al. (1995), "Dopamine neurotoxicity inhibition of mitochondrial respiration," <i>J Neurochem</i> , 64:718-723
	Bergmann, K. J., et al. (1986), "Parkinson's disease and long term levodopa therapy," Adv Neurol, 45:463-467
	Bhakar, A. L., et al. (2002), "Constitutive nuclear factor kappa B activity is required for central neuron survival," <i>J Neurosci</i> , 22(19):8466-8475
	Bodnar, R. J., et al. (1990), "Proglumide selectively potentiates supraspinal mu 1 opioid analgesia in mice," <i>Neuropharmacol</i> , 29(5):507-510
	Brockmoller, J., et al. (2002), "The importance of the CYP2D6 polymorphism on haloperidol pharmacokinetics and on the outcome of haloperidol treatment," <i>Clin Pharmacol & Therap</i> , 72(4):438-452
	Brooks, D. J. and Samuel, M. (2000), "The effects of surgical treatment of parkinson's disease and tremor: articles" <i>Am Acad Neurol</i> , 55(12):S52-S59
	Brooks, D. J., et al. (2000), "Neuroimaging of dyskinesia," <i>Ann Neurol</i> , 47(suppl 1):S154-S159
	Buszman, E., et al. (1984), "Electron spin resonance studies of chloroquine-melanin complexes," <i>Biochem Pharmacol</i> , 33(1):7-11
	Cadet, J. L. and Kahler, L. A. (1989), "Free radical mechanisms in schizophrenia and tardive dyskinesia," <i>Neurosci Behav Rev</i> , 18(4):457-467
	Carta, A., et al. (2002), "Differential regulation of GAD67, enkephalin and dynorphin mRNA by chronic-intermittent l-dopa and A _{2a} receptor blockade plus l-dopa in dopamine-denervated rats," <i>Synapse</i> , 44:166-174
	Chang, K. J., et al. (1982), "Opioid peptides induce reduction of enkephalin receptors in cultured neuroblastoma cells," <i>Nature</i> , 296:446-448
	Chase, T. N. et al. (1986), "Fluctuation in response to chronic levodopa therapy pathogenetic and therapeutic considerations," <i>Adv Neurol</i> , 45:477-480
-	Chen, F. Lu et al. (1997), "Calpain contributes to silica induced I kappa B-alpha degradation and nuclear factor-kappa B activation," <i>Arch Biochem Biophysics</i> , 342(2):383-388
	Chen, F. Lu et al. (1997), "Calpain contributes to silica induced I kappa B-alpha degradation and nuclear factor-kappa B activation," <i>Arch Biochem Biophysics</i> , 342(2):383-388
	Cheng, N. et al. (1996), "Differential neurotoxicity induced by I-dopa and dopamine in cultured striatal neurons," <i>Brain Res</i> , 743(1-2):278-283
	Chiodo, L. A. and Bunney B. S. (1983), "Typical and atypical neuroleptics: differential effects of chronic administration on the activity of A9 and A10 midbrain dopaminergic neurons," <i>J Neurosci</i> , 3(8):1607-1619
	Chugani, D. C. et al. (1988), "In vivo [3H]spiperone binding: evidence for accumulation in corpus striatum by agonist-mediated receptor internalization," <i>J Cereb Blood Flow & Metab</i> , 8(3):291-303
	Cohen, S. N. and Yielding, K. L., (1965), "Inhibition of DNA and RNA polymerase reactions by chloroquine," <i>Proc Natl Acad Sci</i> , 54(2):521-527

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616/692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

	Coleman, T. et al., "1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) is n-
	demethylated by cytochromes P450 2D6, 1A2 and 3A4 –Implications for
	susceptibility to Parkinson's Disease," J. Pharm. And Exp. Therapeutics,
	277(2):685-690
	Conley, R. R., and Buchanan, R. W. (1997), "Evaluation of treatment resistant
	schizophrenia," Schizo Bull, 23(4):663-674
	Cooper, A. and Mitchell, I. (1995), "Fos immuno-positive neurons in the STN
	following reversal of Parkinson's disease symptoms by antagonism of excitatory
	amino acid transmission in the entopeduncular nucleus of the monoamine
	depleted rat," Neurosci Let, 201(3):251-254
	Dahl, M-L, "Cytochrome P450 phenotyping/genotyping in patients receiving
	antipsychotics: useful aid to prescribing," Clin Pharmacokinet, 41(7):453-470
	D'Amato, R. J. et al. (1987), "Characterization of the binding of N-methyl-4-
	phenylpyridine, the toxic metabolite of the parkinsonian neurotoxin N-methyl-4-
	phenyl-1,2,3,6-tetrahydropyridine to neuromelanin," <i>J Neurochem</i> , 48(2):653-658
	Davis, G.C. et al. (1979), "Chronic parkinsonism secondary to intravenous
	injection of meperidine analogues," <i>Psych Res,</i> 1:249-254
	Deutch, A. Y. (1993), "Prefrontal cortical dopamine systems and the elaboration
	of functional corticostriatal circuits: implications for schizophrenia and parkinson's
	disease," J Neural Trans, 91(2-3):197-221
 	
	Doss, R. C. et al. (1981), "Recovery of β-adrenergic receptors following long term
	exposure of astrocytoma cells to catecholamine," <i>J Biol Chem</i> , 258:12281-12286
	Egan, M. F. et al. (1997), "Treatment of tardive dyskinesia," Schizo Bull, 23(4):583-609
	Egan, M. F. et al. (1996), "Pharmacological and neurochemical differences
	between acute and tardive viscous chewing movements induced by haloperidol,"
	Psychopharmacol, 127:337-345
	Elbert, M.H et al. (1984), "Selective neurotoxic effects of n-methyl-4-phenyl-
	1,2,3,6-tetrahydropyridine (MPTP) in subhuman primates and man: a new animal
	model of parkinson's disease," Psychopharmacol Bull, 20(3):548-553
	Essien, E. E. and Ette, E. I., (1986), "Effects of chloroquine and
	didesethylchloroquine on rabbit myocardium and mitochondria," J Pharm
	Pharmacol, (38):543-546
	Essien, E. E. et al. (1989), "Chloroquine disposition in hypersensitive subjects
	and its significance in chloroquine-induced pruritus," Eur J of Drug Metab and
]]	Pharmacokinet, 14(1):71-77
	Ette, E. I. and Essien, E. E. (1986), "Neuromuscular weakness and
	ultrastructural damage produced by desethylated metabolites of chloroquine and
	the reversal by calcium," West African J of Anatomy 1(1):5-15
	Feigenbaum, P. E. and Fakahny, E. E. (1984), "Short term regulation of
	muscarinic acetylcholine receptor grinding in cultured nerve cells," Res Commum
	Chem Pathol Pharmacol, 43:519-522
	Frackiewicz, E. J. et al. (2002), "Brasofensine treatment for parkinson's disease
	in combination with levodopa/carbidopa," <i>Ann Pharmacother</i> , 36(2):225-230
	Fuller R. W. and Hemrick, S. K. (1985), "Effects of amfonelic acid α-
	methyltyrosine, Ro4-1284 and haloperidol pretreatment on the depletion of
	striatal dopamine by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine in mice," Res
	Comm Chem Ophthalmol Pharmacol, 48(1):17-25
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Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616/692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

	T =
	Furukawa, N. et al. (2001), "Endogenously released dopa is causal factor for glutamate release and resultant delayed neuronal bell death by transient ischemia in rat striata," <i>J Neurochem</i> , 76(3):815-824
	Geula, C. et al. (1994), "Cholinesterase activity in the plaques tangles and angiopathy of Alzheimer's disease does not emanate from amyloid," <i>Brain Res</i> ,
	644(2):327-630 Glazer, W. M. et al. (1993), "Predicting the long-term risk of tardive dyskinesia in out-patients maintained on neuroleptic medications," <i>J Clin Psych</i> , 54(4):133-139
	Goodman, R. and Snyder, H. (1982), "K-opiate receptors localized by autography to deep layers of cerebral cortex: relation to sedative effects," <i>Proc Natl Acad Sci USA</i> , 79:5703-5707
	Goshima, Y. et al. (1993), "L-dopa induces Ca(2+)-dependent and tetrodotxin- sensitive release of endogenous glutamate from rat striatal slices," <i>Brain Res</i> , 617(1):167-170
	Herrero, M. T. et al. (1996), "Consequence of nigrostriatal denervation and I-dopa therapy on the expression of glutamic acid decarboxylase messenger RNA in the pallidum," <i>Am Acad Neurol</i> , 47(1):219-224
	Hillier, C. E. et al. (Feb. 1999), "Thalamotomy for severe antipsychotic induced tardive dyskinesia and dystonia," <i>J. Neurol. Neurosurg. Psychiatry</i> 66:250-251
	Hirsch, E. (2000), "Nigrostriatal system plasticity in parkinson's disease: effect of dopaminergic denervation and treatment," <i>Ann Neurol</i> , 47(suppl 1):S155
	Hughes, N. et al. (1998), "Kappa-opioid receptor agonists increase locomotor activity in the monoamine depleted rat model of parkinsonism," <i>Mov Disord</i> , 13(2):228
	Iravani, M. M. et al. (2001), "GDNF reverses priming for dyskinesia in MPTP-treated, I-dopa primed common marmosets," <i>Euro J Neurosci</i> , 13(3):597-608
	Iverson, L.L. and Kelly, J.S. (1975), "Uptake and metabolism of γ-aminobutyric acid by neurons and glial cells, " <i>Biochem Pharmaco</i> , 24:993-998
	Jarosinski, K. W. et al. (2001), "Specific deficiency in nuclear factor κB activation in neurons of the central nervous system," <i>Lab Invest</i> , 81(9):1275-1288
	Jenner, P. (2000), "Factors influencing the onset and persistence of dyskinesia in MPTP treated primates," <i>Ann Neurol</i> , 47(suppl 1):S90-S104
	Jenner, P. (2002), "Pharmacology of dopamine agonists in the treatment of Parkinson's disease," <i>Am Acad Neurol</i> , 58(4):suppl 1 S1-S8
	Jindal, M. N. et al. (1960), "Local anesthetic action of antimalarials (chloroquine and amodiaquine)" <i>Arch Int Pharmacodyn</i> 127:132-140
	Jindal, M. N. (1970), "Adrenergic neurone blockade with chloroquine and amodiaquine," <i>Br J Med</i> , 58(8):1050-1056
	Johansson, P. E. et al. (1990), "Neuropeptide changes in a primate model (cebus apella) for tardive dyskinesia," Neurosci, 37(2):563-567
	Kane, J.M., "Tardive dyskinesia: epidemiological and clinical presentation," (1995) Psychopharmacology: The Fourth Generation of Progress, 1485-1495
	Kingsbury, A. E. et al. (1998), "DNA fragmentation in human substantia nigra: apoptosis or perimortem effect?" <i>Mov Disord</i> , 13(6):877-884
	Klawans, H. and Shenker, D. (1970), "Theoretical implications of the use of I-dopa in parkinsonism," <i>Acta Neurol Scand</i> , 46:409-441
	Klawans, H. L. (1973), "The pharmacology of tardive dyskinesias" <i>Am J Psych</i> , 130(1):82-86

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616/692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

Kure, S. et al. (1991), "Glutamate triggers internucleosomal DNA cleavage in neural cells," <i>Biochem & Biophysical Res Comm</i> , 179(1):39-45
Kurnick, N. B. and Radcliffe, I. E. (1962), "Reaction between DNA and quinacrine and other antimalarials," <i>J Lab & Clin Med</i> , 60(4):669-688
Ladipo, G. O. et al. (1983), "Complete heart block in chronic chloroquine poisoning," Int J Cardiol, 4:198-200
Lang, A. E. (2000), "Surgery for levodopa induced dyskinesias," <i>Ann Neurol</i> , 47(suppl 1): S193-S202
Langston, J.W., (1986) "MPTP-induced Parkinsonism: how good a model is it?" Recent Dev. In Parkinson's Disease, 119-126
Law, P. Y. et al. (1984), "Down-regulation of opiate receptor in neuroblastoma x glioma NG 108-15 hybrid cells," <i>J Biol Chem</i> , 259(14):4096-4104
Lee, H. J. et al. (2001), "Anti-apoptotic role of NF-kappaB in auto-oxidized dopamine induced apoptosis of PC12 cells," <i>Journal of Neurochemistry</i> , 76(2):602-609
Lieberman, J. A. et al. (1997), "Neurochemical sensitization in the pathophysiology of schizophrenia deficits and dysfunction in neuronal regulation and plasticity," <i>Neuropsychopharmacology</i> , 17:205-229
Lim, L. Y. and Go, M. L. (1986), "The anticholinesterase activity of mefloquine," Clin Exp Pharmacol Physiol, 13(6):527-531
Lindefors, N. (1993), "Dopaminergic regulation of glutamic acid decarboxylase mRNA expression and GABA release in the striatum," <i>Prog Neurol Psychopharmacol & Biol Psych</i> , 17(6):887-903
Lipsky, R. H. et al. (2001), "Nuclear factor kappaB is a critical determinant in N-methyl-d-aspartate receptor mediated neuroprotection," <i>J Neurochem</i> , 78(2):254-264
Liu, L. et al.1990), "Interactions of chloroquine with benzodiazepine, gamma-aminobutyric acid and opiate receptors," <i>Biochem Pharma</i> , 41(10):1534-1536
Lozano, A. M. et al. (2000), "Neuronal recording in parkinson's disease patients with dyskinesias induced by apomorphine," <i>Ann Neurol</i> , 47(suppl 1):S142-S146
Luo, J. et al. (2002), "Subthalamic GAD gene therapy in a parkinson's disease rat model," <i>Science</i> , 298(5592):425-429
Maeda, T. et al. (1997). "L-DOPA neurotoxicity is mediated by glutamate release in cultured rat striatal neurons," <i>Brain Res</i> , 771(1):159-162
Maneuf, Y.P. et al., (1995) "Functional implications of kappa opioid receptor-mediated modulation of glutamate transmission in the output regions of the basal ganglia in rodent and primate models of Parkinson's disease," <i>Brain Research</i> 683:102-108
Mangelus, M. et al. (2001), "Involvement of nuclear factor kappa B in endothelin a receptor induced proliferation and inhibition of apoptosis," <i>Cell Mol Neurobiol</i> , (6):657-674
Manson, A.J. et al., "High dose naltrexone for dyskinesias induced by levodopa," (2001) <i>J. Neurol. Neurosurg. Psychiatry</i> 70:554-556
Martin, B. C. et al. (2001), "Antipsychotic prescription use and costs for persons with schizophrenia in the 1990s: current trends and five year time series forecasts," <i>Schizo Res</i> , 47(2-3):281-292

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616/692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

Mavridis, M. and Besson, M. J. (1999), "Dopamine-opiate interaction in the regulation of neostriatal and pallidal neuronal activity as assessed by opioid precursor peptides and glutamate decarboxylase messenger RNA expression," <i>Neurosci</i> , 92(3):945-966
Mitchell, I. J. et al. (1985), "Sites of the neurotoxic action of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine in the macaque monkey include the ventral tegmental area and the locus ceruleus," <i>Neurosci Lett</i> , 61:195-200
Mitchell, I.J. and Carroll, C.B. (1997), "Reversal of Parkinson's disease symptoms in primates by antagonism of excitatory amino acid transmission, potential mechanisms of action," <i>Neurosci & Behav Res</i> , 21(4):469-475
Mitchell, I. J. et al. (1994), "Glutamate-induced apoptosis results in a loss of striatal neurons in the parkinsonian rat," <i>Neurosci</i> , 63(1):1-5
Mitchell, I. J. et al. (1985), "Subcortical changes in the regional uptake of [³ H]-2-deoxyglucose in the brain of the monkey during experimental choreiform dyskinesia elicited by injection of a gamma aminobutyric acid antagonist into the subthalamic nucleus," <i>Brain</i> , 108(Pt.2):405-422
Mitchell, I. J. et al. (1992), "A 2-deoxyglucose study of the effects of dopamine agonists on the parkinsonian primate brain implications for the neural mechanisms that mediate dopamine agonist induced dyskinesia," <i>Brain</i> , (Pt 3):809-824
Mitchell, I. J. et al.(1992), "Regional changes in 2-deoxyglucose uptake associated with neuroleptic induced tardive dyskinesia in the cebus monkey," <i>Mov Disord</i> , 7(1):32-37
Mitchell, I. J. et al. (1986), "Neural mechanisms mediating 1-methyl-4-phenyl-1,2,3,5-tetrahydropyridine-induced parkinsonism in the monkey relative contributions of the striatopallidal and striatonigral pathways as suggested by 2-deoxyglucose uptake," <i>Neurosci Lett</i> , 63:61-65
Mitchell, I. J. et al. (1989), "Neural mechanisms underlying parkinsonian symptoms based upon regional uptake of 2-deoxyglucose in monkeys exposed to 1-methyl-4-phenyl-1,2,6-tetrahydropridine," <i>Neurosci</i> , 32(1):213-226
Miyachi, Y. et al. (1986), "Antioxidant action of antimalarials," <i>Ann Rheum Disease</i> , 45:244-248
Morgenstern, H. and Glazer, W. M. (1993), "Identifying risk-factors for tardive dyskinesia among long-term outpatients maintained with neuroleptic medications," <i>Arch Gen Psych</i> , 50:723-733
Nandi, D. et al. (2002), "Reversal of akinesia in experimental parkinsonism by GABA antagonist microinjections in the pedunculopontine nucleus," <i>Brain</i> , 125(11):2418
Napier, T. C. and Mitrovic, I. (1999), "Opioid modulation of ventral pallidal inputs," NY Acad Sci, 877:176-201
Nutt, J. G. (2000), "Clinical pharmacology of levodopa-induced dyskinesia," <i>Ann Neurol</i> , 47(suppl 1):S160-S166
Obeso, J. et al. (2000), "Pathophysiology of levodopa-induced dyskinesias in parkinson's disease: problems with the current model," <i>Ann Neurol</i> , 47(suppl 1):S22-S34
Ogura, M. and Kita, H. (2000), "Dynorphin exerts both postsynaptic and presynaptic effects in the globus pallidus of the rat," <i>J Neurophysiol</i> , 83(6):3366-3376

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616/692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

Olanow, C.W. and Obeso, J. A. (2000), "Preventing levodopa induced dyskinesias," <i>Ann Neurol</i> , 47(suppl 1):S167-S178
O'Shaughnessy, T.J. et al. (2003, "Acute neuropharmacologic action of
chloroquine on cortical neurons in vitro," Brain Res, 959:280-286
Osifo, N. (1979), "Drug-related transient dyskinesias," Clin Pharma & Therap, 25(6):767-771
Ostermeier, A. et al. (2000), "Activation of mu- and delta-opioid receptors causes presynaptic inhibition of glutamatergic excitation in neocortical neurons," <i>Anesthesiol</i> , 93(4):1053-1063
Pahl, J. L. et al. (1995), "Positron-emission tomography in tardive dyskinesia," <i>J Neuropsych</i> , 7:457-465
Pandya, K. H. et al. (1968), "Mechanism of supersensitivity to catecholamines following chloroquine," <i>Arzneimittelforschung</i> , 18(7):786-790
Perlmutter, J. S. et al. (1997), "MPTP induces dystonia and parkinsonism: clues to the pathophysiology of dystonia," <i>Am Acad Neurol</i> , 49(5):1432-1438
Piccini, P. et al. (1997), "Alterations in opioid receptor binding in parkinson's disease patients with levodopa induced dyskinesias," <i>Ann Neurol</i> , 42(5):720-726
Rascol, O. (2000), "Medical treatment of I-dopa induced dyskinesias," <i>Ann Neurol</i> , 47(suppl 1):S179-S188
Rascol, O. et al. (1994), "Naltrexone, an opiate antagonist, fails to modify motor symptoms in patients with Parkinson's disease," <i>Movement Disorders</i> , 9:437-440
Reddy, R. D. and Yao, J. K. (1996), "Free Radical pathology in schizophrenia: a review," Free Rad Pathol, 33-43
Richardson, P. J. (2001), "The adenosine A _{2A} receptor of the basal ganglia," <i>J Physiol</i> , 532(2):284-288
Rinne, U. K. et al. (1990), "Positron emission tomography demonstrates
dopamine D ₂ receptor supersensitivity in the striatum of patients with early parkinson's disease" <i>Mov Disord</i> , 5(1):55-59
Rinne, U. K. et al. (1983), "Brain enkephalin receptors in parkinson's disease," <i>J Neural Transmiss</i> , Supp. 19:163-171
Rodnitzky, R. L. (2002), "Drug-induced movement disorders," <i>Clin Neuropharmacol</i> , 25(3):142-152
Ross, S. B. (1995), "Comparison of high-affinity binding of ³ H proadifen and ³ H (-)-cocaine to rat live membranes," <i>Pharmacol & Toxicol</i> , 76(2):141-145
Rupp, A. and Keith, S. J. (1993), "The costs of schizophrenia: assessing the burden," <i>Psych Clin N Am</i> , 16:413-423
Sarre, S. et al. (1997), "Biotransformation of locally applied precursors of dopamine, serotonin and noradrenaline in striatum and hippocampus: a
microdialysis study," <i>J Neural Transm</i> , 104:1215-1228 Schwartz, J. C. et al. (1993), "Dopamine D ₃ receptor: basic and clinical aspects,"
Clin. Neuropharmacol. 16(4):295-314
Schwartz, J. C. et al.(1998), "Functional implications of multiple dopamine receptor subtypes: the D ₁ /D ₃ receptor coexistence," <i>Brain Research</i> , 26(2-3):236-242
Seeman, P. and Kapur, S. (1997), "Clozapine occupies high levels of dopamine d2 receptors," <i>Life Sci</i> , 60(12):207-216
Sheridan, R. et al. (1997), "Structural features of aminoquinolines necessary for antagonist activity against botulinum neurotoxin," <i>Toxicon</i> , 34(9):1439-1451

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616/692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

	Shindou, T. et al. (2000), "Adenosine A _{2A} receptor enhances GABA _A -mediated IPSCs in the rat globus pallidus," 532(2):432-434
	Sodeyama, N. et al. (1999), "Association between butyrylcholin-esterase K
	variant and the Alzheimer neuropathological changes in apolipoprotein E (E4)
	carriers older than 75," J Neurol Neurosurg Psych, 67(5):693-694
	Sokoloff, P. et al. (1990), "Molecular cloning and characterization of a novel
	dopamine receptor (D ₃) as a target for neuroleptics," Nature, 347:146-151
	Stanford, I. M. and Cooper, A. J. (1999), "Presynaptic mu and delta opioid
	receptor modulation of GABAa IPSCs in the rat globus pallidus in vitro," J
	Neurosci, 19(12):4796-4803
	Stern, Y. and Langston, J. W. (1985), "Intellectual changes in patients with MPTP-induced parkinsonism," <i>Neurol</i> , 35:1506-1509
	Sugaya, Y. et al. (2001), "Autoradiographic studies using L-[14C]DOPA and –
	[3H]DOPA reveal regional Na ⁺ -dependent uptake of the neurotransmitter
	candidate L-DOPA in the CNS," Neurosci, 104(1):1-14
	Szymanski, S. D. et al. (1996), "Vulnerability to tardive dyskinesia development in
	schizophrenia and FDG-PET study of cerebral metabolism,"
	Neuropsychopharmacol, 15(6):567-575
	Tanaka, M. et al. (2000), "Novel alternative promoters of mouse glial cell line-
	derived neurotrophic factor gene," Biochimica et Biophysica Acta, 1494(1-2):63-
	74
	Tjalve, H. et al. (1981), "Studies on the binding of chlorpromazine and
	chloroquine to melanin in vivo," Biochem Pharmacol, 30(13):1845-1847
	Tseng, L. and Collins, K. (1991), "Involvement of epsilon and kappa opioid
	receptors in the inhibition of the tail flick response induced by phenazocine in the mouse," <i>J Exp Ther</i> , 259:330-336
	Wainer, I. W. et al. (1994), "Distribution of the enantiomers of hydroxychloroquine
	and its metabolites in ocular tissues of the rabbit after oral administration of
	racemic-hydroxychloroquine," Chirality 6:347-354
	Waldmeier, P. C. (2003), "Prospects for anti-apoptotic drug therapy of
	neurodegenerative diseases," Nerv Sys Res, 27(2):303-321
	Weber, S. M. et al. (2002), "Inhibition of mitogen activated protein kinase
	signaling by chloroquine," J Immunol, 168:5303-5309
	Weber, S. and Levitz, S. M. (2000), "Chloroquine interferes with
	lipopolysaccharide-induced TNF-α gene expression by nonlysosomotropic
	mechanisms," <i>J Immunol</i> , 163(3):1534-1540
	Weetman, J. and Anderson, I. M. (1997), "Bilateral posteroventral pallidotomy for
	severe antipsychotic induced tardive dyskinesia and dystonia," J Neurol
<u> </u>	Neurosurg & Psych, 63:417-418
	Weglicki, W. B. et al. (1993), "Modulation of cytokines and myocardial lesions by
	vitamin e and chloroquine in a Mg-deficient rat model," Am. J. Cell Physiol,
	264(3):169-172
	Witiak, D., Grattan, D., Heaslpi, R. and Rahwan, R. (1981), "Synthesis and
	preliminary pharmacological evaluation of asymmetric chloroquine analogues," J
	Med Chem, 24(6):712-717
	Wolters, E. (1999), "Dopaminomimic psychosis in parkinson's disease patients:
u	diagnosis and treatment," Neurol, 52(7):S10-S13

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616/692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

EXAMINER	DATE CONSIDERED
	http://www.ninds.hih.govhealinfo/diorder/parkinso/pdreport/pftherapy.ntm
	research planning workshop,
	"National Institute of Neurological Disorders and Stroke" Parkinson's disease: A
	http://phantom.uchsc.edu/mdxcgi/diSYS&SET=485440&SYS=1&T=358&D=16
	"Chloroquine", "Sinemet" & "Levodopa" MicroMedex Healthcare Series.
	Electronic Resources
	Sigma-Aldrich (2002), "Pain and Mechanisms of Analgesia," Catalog # FIO 356-500947 0112
	Merritt's Textbook of Neurology, (1995), 9 th Ed, Williams & Wilkins, Baltimore, MD, "Movement disorders" pp. 713-730
	Books
	Zamir, N. et al. (1984), "Primate model of parkinson's disease: alterations in multiple opioid systems in the basal ganglia," <i>Brain Res</i> , 322(2):356-360
	primary astrocytes on MAP kinase activation, transcription factor activation and neurotrophin secretion," <i>Neurochem Res</i> , 26(12):1293-1299
	Zaheer, A. et al. (2001), "Effects of glia maturation factor over expression in
	Yu, S. P. et al.(1999), "NMDA receptor mediated K+ efflux and neuronal apoptosis," <i>Science</i> , 284(5412):336-339
	Yu, P. (2002), "Brasofensine neuro search," Cur Opin Invest Drugs, 1(4):504-508
	Youdim, M. B. et al. (1994), "The enigma of neuromelanin in parkinson's disease substantia nigra," <i>J Neural Transm</i> , 43(suppl):113-122
	ganglia of the rat brain by dynorphin peptides," <i>J Pharmacol & Exp Therap</i> 290(3):1307-1315
	the evidence and its therapeutic implications," CNS Drugs, 15(4):287-310 You, Z. B. et al. (1999), "Modulation of neurotransmitter release in the basal
	Yao, J. K. et al. (2001), "Oxidative damage and schizophrenia: An overview of
	effects of pigment epithelium derived factor (PEDF) on cerebellar granule neurons," <i>J Bio Chem</i> , 276(46):43313-43319
	Yabe, T. et al.(2001), "NF kappa B activation is required for the neuroprotective

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

AUG Z 4 ZUIX	307	
Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson	-	GROUP 1614

U.S. PATENT DOCUMENTS

Exmr. Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation Yes/No
		1 1			

OTHER PRIOR ART (including Author, Title, Date, Pertinent Pages, etc.)

1	1	Abiose, A.K. et al., "Chloroquine-induced venodilation in human hand veins," (1997) Clin. Pharm. & Therapeutics 61(6):677-683
2	2	Antonini, A. et al., "Differential diagnosis of Parkinsonism with [18F]Fluorodeoxyglucose and PET," (1998) Movement Disorders 13(2):268-274
2	2A	Ardueser, G.A. and Heim, H.C., "Some effects of chloroquine on oxidative processes in rat heart," (1967) <i>J. Pharmaceutical Sciences</i> 56(2) :254-258
3	3	Baltzan, M. et al., "Randomized trial of prolonged chloroquine therapy in advanced pulmonary sarcoidosis," (1999) Am. J. Respir. Crit. Care Med. 160:192-197
4	4	Behl, C. et al., "Hydrogen peroxide mediates amyloid β protein toxicity," (1994) <i>Cell</i> 77:817-827
5	5	Ben-Shachar, D. and Youdim, M.B.H., "Selectivity of melaninized nigra-striatal dopamine neurons to degeneration in Parkinson's disease may depend on iron-melanin interaction," (1990) J. Neural Transm. 29:251-258
6	6	Ben-Shachar, D. et al., "The iron chelator desferrioxamine (Desferal) retards 6-hydroxydopamine-induced degeneration of nigrostriatal dopamine neurons," (1991) J. Neurochemistry 56(4) :1441-1444
7	7	Bergendi, L'. et al., "Chemistry, physiology and pathology of free radicals," (1999) <i>Life Sciences</i> 64(18-19) :1865-1874
8	8	Bitonti, A.J. et al., "Reversal of chloroquine resistance in malaria parasite <i>plasmodium</i> falciparum by desipramine," (1988) Science 241:1301-1303

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson		GROUP 1614

·		
	8A	Booij, J. et al., "[123I]FP-CIT SPECT shows a pronounced decline of striatal dopamine transporter labelling in early and advanced Parkinson's disease," (1997) J. Neurol. Neurosurg. Psychiatry 62:133-140
	9	Bowen, B.C. et al., "Proton MR spectroscopy of the brain in 14 patients with Parkinson's disease," (1995) Am. J. Neuroradiology 161(1):61-68
	10	Burke, R.E., "Programmed cell death and Parkinson's disease," (1998) Movement Disorders 13(S1):17-23
	11	Byrd, T.F. and Horowitz, M.A., "Chloroquine inhibits the intracellular multiplication of Legionella pneumophila by limiting the availability of iron. A potential new mechanism for the therapeutic effect of chloroquine against intracellular pathogens," (1991) J. Clin. Investigation 88(1);351-357
	12	Carlsson, Arvid, "Development of new pharmacological approaches in Parkinson's disease," (1986) Advances in Neurology 45:513-518
	13	Chan, P.C. and Bielski, B.H., "Enzyme-catalyzed free radical reactions with nicotinamide adenine nucleotides. II. Lactate dehydrogenase-catalyzed oxidation of reduced nicotinamide adenine dinucleotide by superoxide radicals generated by xanthine oxidase," (1974) J. Biol. Chem. 249(4):1317-1319
	14	Cho, Y.W. and Aviado, D.M., "Pathologic physiology and chemotherapy of plasmodium berghei. IV. Influence of chloroquine on oxygen uptake of red blood cells infected with sensitive or resistant strains," (1968) Exp. Parasitology 23(2):143-150
-	15	Chrichton, R.R. and Ward, R.J., "Iron metabolism - new perspectives in view," (1992) Biochemistry 31(46):11255-11264
	16	Chrischilles, E.A. et al., "The health burdens of Parkinson's disease," (1998) Movement Disorders 13(3):406-413
	17	Cotzias, G.C. et al., "Melanogenesis and extrapyramidal diseases," (1964) Chemistry in Medicine 23:713-718
	18	Culvenor, J.G. et al., "Non-Aβ component of Alzheimer's disease amyloid (NAC) revisited," (1999) Am. J. Pathology 155:1173-1181
	19	Cummings, J.L., "Depression and Parkinson's Disease: A Review," (1992) Am. J. Psychiatry 149(4):443-454
	. 20	Dailly, E. et al., "Chain-breaking antioxidants and ferriheme-bound drugs are synergistic inhibitors of erythrocyte membrane peroxidation," (1998) Free Radical. Res. 28(2):205-214

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson		GROUP 1614

1		
	21	D'Amato, R.J. et al., "Selectivity of the Parkinsonian neurotoxin MPTP: toxic metabolite MPP+ binds to neuromelanin," (1986) Science 231:987-989
	22	D'Amato, R.J. et al., "Evidence for neuromelanin involvement in MPTP-induced neurotoxicity," (1987) <i>Nature</i> 327 :324-326
	23	Davison, A.J. and Gee, P., "Redox state of cytochrome C in the presence of the 6-hydroxydopamine/oxygen couple: oscillations dependent on the presence of hydrogen peroxide or superoxide," (1984) <i>Arch. Biochem. and Biophysics</i> 233(2):761-771
	24	Debing, I. et al., "Melanosome binding and oxidation-reduction properties of synthetic L-dopa-melanin as in vitro tests for drug toxicity," (1988) <i>Mol. Pharmacology</i> 33(4):470-476
	25	De Duve, C. et al., "Lysosomotropic agents," (1974) Biochem. Pharm. 23:2495-2531
	26	Deepalakshmi, P.D. et al., "Effect of chloroquine on rat liver mitochondria," (1994) <i>Indian J. Exp. Biology</i> 32(11) :797-799
	27	De Feo, P. et al., "Chloroquine reduces whole body proteolysis in humans," (1994) Am. J. Physiology 267:E183-E186
	28	Dethy, S. et al., "Asymmetry of basal ganglia glucose metabolism and dopa responsiveness in Parkinsonism," (1998) <i>Movement Disorders</i> 13(2) :275-280
	29	Dexter, D.T. et al., "Basal lipid peroxidation in substantia nigra is increased in Parkinson's disease," (1989) J. Neurochem. 42(2):381-389
	30	Di Monte, D.A. et al., "Astrocytes as the site for bioactivation of neurotoxins," (1996) NeuroToxicology 17(3-4):697-704
	31	Farid, M.A., "The malaria campaign - why not eradication?" (1998) World Health Forum 19:417-427
	32	Fridovich, I., "Superoxide dismutases," (1975) 147-159
	33	Fukushima, T. et al., "Radical formation site of cerebral complex I and Parkinson's disease," (1995) J. Neuroscience Res. 42:385-390
	34	German, D.C. et al., "1-methyl-4-phenyl-1,2,3,6-tetra-hydropyridine-induced Parkinsonian syndrome in <i>macaca faxcicularis</i> : which midbrain dopaminergic neurons are lost?" (1988) <i>Neuroscience</i> 24(1) :161-174
	35	Ghigo, D. et al., "Chloroquine stimulates nitric oxide synthesis in murine, porcine, and human endothelial cells," (1998) J. Clin. Invest. 102(3):595-605

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson		GROUP 1614

	~
36	Gibb, W.R.G. and Lees, A.J., "Anatomy, pigmentation, ventral and dorsal subpopulations of the substantia nigra, and differential cell death in Parkinson's disease," (1991) J. Neurology, Neurosurgery, and Psychiatry 54:388-396
37	Glinka, Y.Y. and Youdim, M.B.H., "Inhibition of mitochondrial complexes I and IV by 6-hydroxydopamine," (1995) Eur. J. Pharmacology Environ. Toxicol. Pharmacol. Section 292, 329-332
38	Glinka, Y. et al., "Nature of inhibition of mitochondrial respiratory complex I by 6-hydroxydopamine," (1996) J. Neurochemistry 66(5):2004-2010
39	Golbe, L.I., "Alpha-synuclein and Parkinson's disease," (1999) Movement Disorders 14(1):6-9
40	Goldstein, M. and Lieberman, A., "The role of the regulatory enzymes of catecholamine synthesis in Parkinson's disease," (1992) Neurology 42(S4):8-12
41	Gotham, A.M. et al., "Levodopa treatment may benefit or impair 'frontal' function in Parkinson's disease," (1986) <i>Lancet</i> 25;2(8513) :970-971
42	Graham, D., "Catecholamine toxicity: A proposal for the molecular pathogenesis of manganese neurotoxicity and Parkinson's disease," (1984) <i>Toxicology</i> 5(1) :83-96
43	Graham, D.G., "Oxidative pathways for catecholamines in the genesis of neuromelanin and cytotoxic quinones," (1978) Molecular Pharmacology 14:633-643
44	Graham, D.G., "Autoxidation versus covalent binding of quinones as the mechanism of toxicity of dopamine, 6-hydroxydopamine, and related compounds toward C1300 neuroblastoma cells in vitro" (1978) Molecular Pharmacology 14:644-653
45	Hall, S. et al., "MRI, brain iron and experimental Parkinson's disease," (1992) J. Neurological Sci. 198-208
46	Hirsch, E. et al., "Melanized dopaminergic neurons are differentially susceptible to degeneration in Parkinson's disease," (1988) <i>Nature</i> 334 :345-348
47	Hirsch, E.C. and Faucheux, B.A., "Iron metabolism and Parkinson's disease," (1998) Movement Disorders 13(S1):39-45
48	Ivanina, T.A. et al., "A study of the mechanisms of chloroquine retinopathy," (1989) Ophthalmic Res. 21:216-220
49	Ivanova, S. et al., "Cerebral ischemia enhances polyamine oxidation: identification of enzymatically formed 3-aminopropanal as an endogenous mediator of neuronal and glial cell death," (1998) J. Exp. Med. 188(2):327-340
50	Jackson, M.J. et al., "Inhibition of lipid peroxidation in muscle homogenates by phospholipase A2 inhibitors," (1984) <i>Bioscience Reports</i> 4(7) :581-587 (abstract only)

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson		GROUP 1614

	T
51	Jenner, P., "Oxidative stress in Parkinson's disease and other neurodegenerative disorders," (1996) <i>Pathologie Biologie</i> 44(1) :57-64
52	Jenner, P. et al., "Understanding cell death in Parkinson's disease," (1998) Annals of Neurology 44(1):S72-S84
53	Karmazyn, M. et al., "The mechanism of coronary artery spasm: roles of oxygen, prostaglandins, sex hormones and smoking," (1979) Medical Hypothesis 5:447-452
54	Kienzl, E. et al., "Iron as catalyst for oxidative stress in the pathogenesis of Parkinson's disease?" (1999) <i>Life Sci</i> 65(18-19):1973-1976
55	Koller, W.C., "When does Parkinson's disease begin?", (1992) Neurology 42(S4):27-31
56	Krogstad, D.J. and Schlesinger, P.H., "Acid-vesicle function, intracellular pathogens, and the action of chloroquine against <i>plasmodium falciparum</i> ," (1987) <i>N.E. J. Med.</i> 317(9):543-549
57	Langston, J.W. et al., "Pargyline prevents MPTP-induced Parkinsonism in primates," (1984) Science 225:1480-1482
58	Langston, J.W., "MPTP neurotoxicity: an overview and characterization of phases of toxicity," (1985) <i>Life Sciences</i> 36 :201-206
59	Larsson, B. and Tjälve, H., "Studies on the mechanism of drug-binding to melanin," (1979) Chemical Pharmacology 28:1181-1187
60	Leahy, F. et al., "Desquamative interstitial pneumonia responsive to chloroquine," (1985) Clinical Pediatrics 24(4):230-232
61	Legssyer, R. et al., "Effect of chronic chloroquine administration on iron loading in the liver and reticuloendothelial system and on oxidative responses by the alveolar macrophages," (1999) <i>Biochem. Pharmacology</i> 57(8):907-911
62	Lieberman et al., "Does selegiline provide a symptomatic or a neuroprotective effect?", (1992) Neurology 42(S4):41-48
63	Lin, A.M-Y et al., "Striatal dopamine dynamics are altered following an intranigral infusion of iron in adult rats," (1998) Free Radical Biology & Medicine 24(6):988-993
64	Linnik, M.D. et al., "Evidence supporting a role for programmed cell death in focal cerebral ischemia in rats," (1993) <i>Stroke</i> 24(12) :2002-2009
65	Loo, D.T. et al., "Apoptosis is induced by β-amyloid in cultured central nervous system neurons," (1993) <i>Proc. Natl. Acad. Sci. USA</i> 90:7951-7955
66	Lyden, A. et al., "Studies on the melanin affinity of haloperidol," (1982) Arch. Int. Pharmacodyn. Ther. 259(2):230-243

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson		GROUP 1614

67	Magwere, T. et al., "Effects of chloroquine treatment on antioxidant enzymes in rat liver and kidney," (1997) Free Radical Biology & Medicine 22(1-2):321-327
68	Makarenko, I.E. and Levitsky, E.P., "Resoquin in the clinic of internal illnesses, and the possible side effects of its use," (1950)
69	Maret, G. et al., "The MPTP story: MAO activates tetrahydropyridine derivatives to toxins causing Parkinsonism," (1990) Drug Metabolism Reviews 22(4):291-332
70	Martin, W.R.W. et al., "Increasing striatal iron content associated with normal aging," (1998) Movement Disorders 13(2):281-286
71	Matsubara, K. et al., "Beta-carbolinium cations, endogenous MPP* analogs, in the lumbar cerebrospinal fluid of patients with Parkinson's," (1995) Neurology 45(12):2240-2245
72	Meerson, F.Z. et al., "Prevention of stress disorders of myocardial contractile function using membrane protectors," (1983) <i>Kardiologiia</i> 23 (7):86-90 (abstract and translation in English)
72A	Mena, M.A., "Pharmacokinetics of L-DOPA in patients with Parkinson's Disease," (1986) Advances in Neurology 45:481-486
73	Merad-Boudia, M. et al., "Mitochondrial impairment as an early event in the process of apoptosis induced by glutathione depletion in neuronal cells: relevance to Parkinson's disease," (1998) <i>Biochem. Pharmacology</i> 56 :645-655
74	Mielke, J.G. et al., "Chloroquine administration in mice increases beta-amyloid immunoreactivity and attenuates kainate-induced blood-brain barrier dysfunction," (1997) Neuroscience Lett. 227(3):169-172
74A	Minotti, G. and Aust, S.D., "The requirement for iron (III) in the initiation of lipid peroxidation by iron (II) and hydrogen peroxide," (1987) <i>J. Biological Chemistry</i> 262(3) :1-98-1104
75	Mizuno, Y. et al., "Mitochondrial dysfunction in Parkinson's disease," (1998) Annals of Neurology 44(S1):S99-S109
76	Monteiro, H.P. and Winterbourn, C.C., "6-hydroxydopamine releases iron from ferritin and promotes ferritin-dependent lipid peroxidation," (1989) <i>Biochem. Pharm.</i> 38(23) :4177-4182
77	Mytilineou, C. et al., "L-(—)-desmethylselegiline, a metabolite of selegiline [L-(—)-deprenyl], protects mesencephalic dopamine neurons from excitotoxicity in vitro," (1997) J. Neurochemistry 68(1):434-436
78	Navas, P. et al., "Decrease of NADH in HeLa cells in the presence of transferrin or ferricyanide," (1986) Biochem. and Biophys. Res. Communications 135(1):110-115

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson	-	GROUP 1614

 r	
79	Nicklas, W.J. et al., "Inhibition of NADH-linked oxidation in brain mitochondria by 1-methyl-4-phenyl-pyridine, a metabolite of the neurotoxin, 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine," (1985) <i>Life Sciences</i> 36 :2503-2508
80	Okamoto, M. et al., "Internucleosomal-DNA cleavage involved in ischemia-induced neuronal death," (1993) <i>Biochem. and Biophys. Res. Communications</i> 196(3) :1356-1362
81	Octave, J-N et al., "Iron uptake and utilization by mammalian cells. I: Cellular uptake of transferrin and iron," (1983) TIBS 217-220
82	Olanow, C.W. and Calne, D., "Does selegiline monotherapy in Parkinson's disease act by symptomatic or protective mechanisms?" (1992) Neurology 42(S4):13-26
83	Ornstein, M.H. and Sperber, K., "The antiinflammatory and antiviral effects of hydroxychloroquine in two patients with acquired immunodeficiency syndrome and active inflammatory arthritis," (1996) <i>Arthritis Rheum.</i> 39(1) :157-161
84	Poewe, W.H. and Wenning, G.K., "The natural history of Parkinson's disease," (1998) <i>Annals of Neurology</i> 44(S1) :S1-S9
85	Pratt, W.B. and Fekety, R., "Chemotherapy of malaria," The Antimicrobial Drugs, (1986) Oxford University Press, New York, Chapter 14:355-384
86	Remblier, C. et al., "Lactic acid-induced increase of extracellular dopamine measured by microdialysis in rat striatum: evidence for glutamatergic and oxidative mechanisms," (1999) Brain Research 837:22-28
87	Riederer, P. et al., "Transition metals, ferritin, glutathione, and ascorbic acid in Parkinsonian brains," (1989) J. Neurochemistry 52(2) :515-520
88	Rollema, H. et al., "In vivo intracerebral microdialysis studies in rats of MPP ⁺ analogues and related charged species," (1990) <i>J. Med. Chem.</i> 33 :221-2230
89	Rollema, H. et al., "MPP ⁺ -like neurotoxicity of a pyridinium metabolite derived from haloperidol: <i>In vivo</i> microdialysis and <i>in vitro</i> mitochondrial studies," (1994) <i>J. Pharm. and Exp. Therapeutics</i> 268(1) :380-387
89A	Rollema, H. et al., "Comparison of the effects of intracerebrally administered MPP ⁺ (1-methyl-4-phenylpyridinium) in three species: microdialysis of dopamine and metabolites in mouse, rat and monkey striatum," (1989) <i>Neuroscience Letters</i> 106 :275-281
90	Roos, R.A. et al., "Response fluctuations in Parkinson's disease," (1990) Neurology 40(9):1344-1346
91	Schapira, A.H., "Oxidative stress in Parkinson's disease," (1995) Neuropathol. Appl. Neurobiol. 21(1):3-9

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson		GROUP 1614

02	
92	Spencer, J.P.E. et al., "Superoxide-dependent depletion of reduced glutathione by L-DOPA and dopamine. Relevance to Parkinson's disease," (1995) <i>NeuroReport</i> 6:1480-1484
93	Sperber, K. et al., "Hydroxychloroquine treatment of patients with human immunodeficiency virus type 1," (1995) Clinical Therapeutics 17(4):622-636
94	Springer, C. et al., "Chloroquine treatment in desquamative interstitial pneumonia," (1987) Archives of Disease in Childhood 62:76-77
95	Stepien, K.B. and Wilczok, T., "Studies of the mechanism of chloroquine binding to synthetic DOPA-melanin," (1982) <i>Biochem. Pharmacol.</i> 1;31(21):3359-3365
96	Stoof, J.C. et al., "Leads for the development of neuroprotective treatment in Parkinson's disease and imaging methods for estimating treatment efficacy," (1999) <i>Eur. J. Pharmacol.</i> 375(1-3):75-86
97	Swaiman, K.F. and Machen, V.L., "Chloroquine reduces neuronal and glial iron uptake," (1986) J. Neurochemistry 46(2):652-654
98	Tipton, K.F. and Singer, T.P., "Advances in our understanding of the mechanisms of the neurotoxicity of MPTP and related compounds," (1993) <i>J. Neurochem.</i> 61(4) :1191-1206
99	Tjalve, H. et al., "Studies on the binding of chlorpromazine and chloroquine to melanin in vivo," (1981) <i>Biochem. Pharmacol.</i> 30(13) :1845-1847
100	Toole-Simms, W. et al., "Transplasma membrane electron and proton transport is inhibited by chloroquine," (1990) <i>Biochem. International</i> 21(4) :761-769
101	Vainshtok, A.B., "Treatment of Parkinsonism with delagil," (1972) Klin. Med (Mosk) 50(9):51-56
102	Yong, V.W. et al., "Depletion of glutathione in brainstem of mice caused by N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine is prevented by antioxidant pretreatment," (1986) Neuroscience Letters 63:56-60
103	Youdim, M.B.H. et al., "Is Parkinson's disease a progressive siderosis of substantia nigra resulting in iron and melanin induced neurodegeneration?", (1989) <i>Acta Neurol. Scand.</i> 126:47-54
104	Biochemistry, (1975) Lubert Stryer, Stanford University, W.H. Freeman and Company, San Francisco, CA
105	"Chloroquine", Micromedex Healthcare Series, http://phantom.uchsc.edu/mdxcgi/diSYS&SET=485440&SYS=1&T=358&D=1692

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson		GROUP 1614

106	Clinical Toxicology of Commercial Products (1984) Gosselin, Smith, Hodge, 5 th Ed., Williams & Wilkins, Baltimore/London, II-245
107	<u>Diagnostic Clinical Neuropsychology</u> (1997) Bigler, E. and Clement, P., 3 rd Ed., University of Texas Press, Austin, TX
108	Fundamentals of Anatomy & Physiology (1995) Martini, Frederic H., 3 rd Ed., Prentice Hall, Englewood Cliffs, NJ
109	The Merck Index, (1996) 12 th Ed., Susan Budavari, Ed., Merck Research Laboratories, Inc., Whitehouse Station, NJ, "Chloroquine - 7-chloro-4-(4-diethylamino-1 methylbutylamino)quinoline," p. 2220
109 A	The Merck Index, (1960) 7th Ed., P.G. Stecher, Ed., Merck & Co., Inc. Rahway, NJ
110	Organic Chemistry, (1996) McMurry, John, 4th Ed., Brooks/Cole Publishing, an International Thomson Publishing Co., Pacific Grove, CA
111	Physicians' Desk Reference, (1996) 50th Ed., Medical Economics Company, Inc., Montvale, NJ
112	Physicians' Desk Reference, (2000) 54th Ed., Medical Economics Company, Inc., Montvale, NJ
113	"Practical chemotherapy of Malaria," (1990) World Health Org. Technical Report Series No. 805, p. 141
113 A	Russian Drug Index, 2d Ed., S. Jablonski, US Dept. HEW, Public Health Service Publication No. 814 (Revised 1967)
114	Textbook of Medical Physiology (1996) Guyton, A.C. and Hall, J.E., 9th Ed., W.B. Saunders Company, Philadelphia, PA

EXAMINER

DATE CONSIDERED

***EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Form PTO 1449 PRADEMAR		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson		GROUP 1614

U.S. PATENT DOCUMENTS

Exmr. Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	6,015,555	01/18/00	Friden (abstract only)	424	133.1	
	5,948,791	09/07/99	Hofheinz et al.	514	313	
	5,834,505	11/10/98	Peters	514	454	
	5,736,556	04/07/98	Moldt et al.	514	304	
	5,639,737	06/17/97	Rubin	514	53	
	5,624,938	04/29/97	Pernis	514	313	
	5,596,002	01/21/97	Hofheinz et al.	514	313	
	5,430,039	07/04/95	Roberts-Lewis et al.	514	297	
	5,210, 076	05/11/93	Berliner et al.	514	21	
	4,421,920	12/20/83	Baudouin et al.	546	163	

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation Yes/No

OTHER PRIOR ART (including Author, Title, Date, Pertinent Pages, etc.)

Augustijns, P. et al., "Stereoselective de-ethylation of chloroquine in rat liver microsomes," (1999) Eur. J. Drug Metabolism & Pharmacokinetics 24(1):105-108 (abstract only)
Augustijns, P. and Verbeke, N., "Stereoselective pharmacokinetic properties of chloroquine and de-ethyl-chloroquine in humans," (1993) Clin. Pharmacokinetics 24(3):259-269 (abstract only)
 Begley, D.J., "The blood-brain barrier: principles for targeting peptides and drugs to the central nervous system," (1996) J. Pharm. Pharmacol. 48(2):136-146
De Boer, A.G. and Breimer, D.D., "The blood-brain barrier: clinical implications for drug delivery to the brain," (1994) J. R. Coll. Physicians Lond. 28(6):50-506

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT Nelson		GROUP 1614

Donatelli, P. eta l., "Stereoselective inhibition by chloroquine of histamine N-methyltransferase in the human liver and brain," (1994) Eur. J. Clin. Pharmacol. 47(4):345-349 (abstract only)
Ducharme, J. et al., "Enantioselective disposition of hydroxychloroquine after a single oral dose of the racemate to healthy subjects," (1995) <i>Brit. J. Clin. Pharmacol.</i> 40(2) :127-133 (abstract only)
Ducharme, J. and Farinotti, R., "Clinical pharmacokinetics and metabolism of chloroquine. Focus on recent advances," (1996) Clin. Pharmacokinet. 31(4):257-74 (abstract only)
Scaria, P.V. et al., "Differential binding of the enantiomers of chloroquine and quinacrine to polynucleotides: implications for steroselective metabolism," (1993) <i>Biopolymers</i> 33(6):887-95 (abstract only)
Tago, C.N. and Ofori-Adjei, D., "Effects of chloroquine and its enantiomers on the development of rat embryos in vitro," (1995) <i>Teratology</i> 52(3) :137-142 (abstract only)
Yatin, S.M. et al., "Alzheimer's amyloid beta-peptide associated free radicals increase rat embryonic neuronal polyamine uptake and ornithine decarboxylase activity: protective effect of vitamin E," (1999) Neuroscience Letters 263(1):17-20 (abstract only)

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

U.S. PATENT DOCUMENTS

Exmr. Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	5,154,924	10/13/02	Friden	424	85.91	

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation Yes/No
William -					

OTHER PRIOR ART (including Author, Title, Date, Pertinent Pages, etc.)

Ambrozi et al. (1976) "L-Dopa and (-)-deprenil in the treatment of Parkinson's disease: long-term study," <i>Br. J. Pharmacol.</i> 58 (3):423-424. Database CA on STN. Chem. Abstr., Vol. 86 (Columbus OH USA), abstract No. 133721
Golbe et al. (1993) "Vitamin E and Parkinson's disease," Vitam. E Health Dis., Packer et al. Eds., Dekker, New York, NY, pp. 787-797, Database CA on STN. Chem. Abstr., Vol. 119 (Columbus, OH, USA) abstract No. 71356
Hemmer et al. (1967) "Cerebral activity of an herbal preparation (Tebonin) from Ginko biloba," Arzneim-Forsch, 17(4):491-493, Database CA on STN. Chem. Abstr., Vol. 67 (Columbus, OH, USA) abstract No. 52644

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003	
	APPLICANT J. Nelson		GROUP 1614	

Cited by Examiner in 09/615,639

U.S. PATENT DOCUMENTS

			TATENT BOOK			
Exmr. Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation Yes/No

OTHER PRIOR ART (including Author, Title, Date, Pertinent Pages, etc.)

Montrastruc JL, 1991. Therapie, 46(4):293-303. Recent advances in the clinical pharmacology of Parkinson's disease.
Lowrey BS, 1997, Pigment Cell Res. vol. 10(5):251-256. Modeling drug-melanin interaction with theoretical linear solvation energy relationships.
Paramar RC et al. 2000, J. Postgrad Med. 46(1):29-30. Chloroquine induced parkinsonism.
Webster et al., Biochem. Pharmacol. 1991, Vol. 42, pages S225-7. Antimalarial activity of optical isomers of quinacrine dihydrochloride against chloroquine-sensitive and resistant plasmodium faciparum <i>in vitro</i> .
Haberkorn A et al., Tropenmed. Parasitol. 1979, Vol. 30, pages 308-312. Antimalarial activity of the optical isomers of chloroquine diphosphate.

EXAMINER

DATE CONSIDERED

***EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

U.S. PATENT DOCUMENTS

Exmr. Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Subclass	Translation Yes/No
					-	

OTHER PRIOR ART (including Author, Title, Date, Pertinent Pages, etc.)

Aisen, Paul S. (1997) "Inflammation and Alzheimer's Disease: Mechanisms and Therapeutic Strategies," <i>Gerontology</i> 43:143-149
Bhatia, M.S. (1991), "Chloroquine-induced psychiatric complications," <i>British Journal of Psychiatry</i> 159(Nov):735 (Abstract)
Bhatia, M.S. et al. (1988), "Capgras syndrome in chloroquine induced psychosis," Indian Journal of Psychiatry 30(3):311-313 (Abstract)
Cockroft, K M. et al. (1996) "Cerebroprotective effects of aminoquanidine in a rodent model of stroke," <i>Stroke</i> 27(8):1393-1398
Conference Proceedings, Stroke Drug Development: Bridging the Gap From Animal Research to Human Trials, March 6-7, 1999, Orlando, FL, Proceedings Transcripts, Side 2, #10
Donatelli, P. et al. (1994) "Stereoselective inhibition by chloroquine of histamine N-methyltransferase in the human liver and brain," Eur. J. Clin. Pharmacol. 47:345-349
Feuerstein, G.Z. and Wang, X. (2000) "Animal models of stroke," <i>Molecular Medicine Today</i> 6:133-135
Garg, P. et al. (1990) "Toxic psychosis due to chloroquine - not uncommon in children," Clinical Pediatrics 29(8):448-450
Golden, G.T. (1992) "Systemic chloroquine protects against striatal dopamine depleciton induced by unilateral intra-nigral MPP+ injection in rats," Soc. Neurosci., (Abstract); letter from Dr. G.M. Alexander in regard thereto.
Good, M.I. and Shader, R.I. (1997) "Behavioral toxicity and equivocal suicide associated with chloroquine and its derivatives," <i>Am. J. Psychiatry</i> 134(7):798-801

Form PTO 1449		
ATTY DOCKET NO. 47-00B	SERIAL NO. 10/616,692	FILING DATE July 9, 2003
APPLICANT J. Nelson		GROUP 1614

	Good, M.I. and Shader, R.I.(1982) "Lethality and behavioral side effects of chloroquine," J. Clin. Psychopharmacology 2:40-46
	Hagihara, N. et al. (2000) "Vascular protection by chloroquine during brain tumor therapy with Tf-CRM107," Cancer Res. 60:230-234
	Lovestone, S. (1991), "Chloroquine-induced mania," British Journal of Psychiatry 159(Jul):164-165 (Abstract)
	Lowrey, A.H. et al., (1997) "Modeling Drug-melanin Interaction with Theoretical Linear Solvation Energy Relationships," <i>Pigment Cell Res.</i> 10_251-256
	Ofori-Adjei, D. et al. (1986) "Enantioselective analysis of chloroquine and desethylchloroquine after oral administration of racemic chloroquine," <i>Therapeutic Drug Monitoring</i> 8:457-461
	Ofori-Adjei, D. et al. (1986) "Protein binding of chloroquine enantiomers and desethyl-chloroquine," <i>Br. J. Clin. Pharmac.</i> 22:356-358
	Rosner, P.I. and Legros, J. (1967) "Hydroxychloroquine et resistance corticale a l'anoxie asphyxique," <i>Therapie</i> XXII:355-360
	Sharma, O.P. (1998) "Effectiveness of chloroquine and hydroxychloroquine in treating selected patients with sarcoidosis with neurological involvement," <i>Archives of Neurology</i> 55(9):1248-1254
	Shields, D.C. et al., (1999) "A putative mechanism of demyelination in multiple sclerosis by proteolytic enzyme, calpain," <i>Proc. Natl. Acad. Sci. USA</i> 96:11486-11491
	Tedeschi, M. (1983), "A case of acute psychosis due to Chloroquine," <i>Information Psychiatrique</i> 59(9):1191-1197 (Abstract)
	Webster, R.V. et al. (1991) "Antimalarial activity of optical isomers of quinacrine dihydrochloride against chloroquine-sensitive and -resistant <i>Plasmodium falciparum in vitro</i> ," <i>Biochem. Pharm.</i> 42:S225-S227

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.